Notice of Allowability	Application No.	Applicant(s)	
	10/816,306	KELLER ET AL.	
	Examiner	Art Unit	
	Amanda L. Lauritzen	3737	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *the amendment filed 07 October 2008*.

2. ☒ The allowed claim(s) is/are *1, 2, 4-7, 9-11 and 13-25*.

3. ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☒ All b) ☐ Some* c) ☐ None of the:
      1. ☒ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☒ Interview Summary (PTO-413), Paper No./Mail Date *20080617-A* .
7. ☒ Examiner's Amendment/Comment
8. ☐ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

/Ruth S. Smith/
Primary Examiner, Art Unit 3737

This action is in response to communications filed 07 October 2008. Claim amendments in that submission are not interpreted to introduce new matter.

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Edward J. Callaghan (Reg. No. 46,594) on 18 December 2008.

The application has been amended as follows:

Please replace claims 1, 2, 4, 5, 7, 9, 13-17, 19-22 and 24, cancel claims 8 and 12, and enter new claim 25 as follows.

1. A device for measuring blood flow in an organ using an injected indicator comprising:

a radiation source for emitting near infrared radiation into tissue of the organ at a first location;

a sensor for detecting a proportion of the emitted near infrared radiation that exits from the organ at a second location; and

an evaluation unit that detects the proportion of the emitted near infrared radiation that exits from tissue of the organ as a single input signal, said evaluation unit being programmed to perform the following evaluation steps:

(a) dividing up said single input signal into a pulsatile component and a non-pulsatile component;

(b) determining an ~~determination of~~ injected indicator concentration with reference to the organ tissue from said non-pulsatile component of said single input signal;

(c) iteratively determining ~~iterative determination~~, from said non-pulsatile component, ~~of~~ an inflow function i(t) that characterizes blood flow through the organ by incrementally varying a mean transit time mtt until a stop criterion is reached;

(d) determining an ~~determination of~~ injected indicator concentration with reference to blood volume in the organ from

said pulsatile component of said single input signal and the iteratively determined inflow function i(t);

(e) calculating a ~~calculation of~~ blood volume in the organ as a quotient of the injected indicator concentration with reference to the organ tissue and the injected indicator concentration with reference to the blood volume in the organ; and

(f) calculating a ~~calculation of the~~ blood flow in the organ as a quotient of the blood volume in the organ and the mean transit time mtt when the stop criterion has been reached.

2. A device for measuring blood flow in an organ using an injected indicator comprising:

a radiation source for emitting near infrared radiation into tissue of the organ at a first location;

a sensor for detecting a proportion of the emitted near infrared radiation that exits from the organ at a second location; and

an evaluation unit that detects the proportion of the emitted near infrared radiation that exits from tissue of the organ as a single input signal, said evaluation unit being programmed to perform the following evaluation steps:

(a) dividing up said single input signal into a pulsatile component and a non-pulsatile component;

(b) determining an ~~determination of~~ injected indicator concentration with reference to the organ tissue from said non-pulsatile component of said single input signal;

(c) iteratively determining ~~iterative determination~~, from said non-pulsatile component, ~~of~~ an inflow function i(t) that characterizes blood flow through the organ by incrementally varying a mean transit time mtt until a stop criterion is reached;

(d) determining an ~~determination of~~ injected indicator concentration with reference to blood volume in the organ from said pulsatile component of said single input signal and the iteratively determined inflow function i(t);

(e) calculating a ~~calculation of~~ blood volume in the organ as a quotient of the injected indicator concentration with reference to the organ tissue and the injected indicator concentration with reference to the blood volume in the organ;

(f) calculating a ~~calculation of the~~ blood flow in the organ as a quotient of the blood volume in the organ and the mean transit time mtt when the stop criterion has been reached; and

(g) scaling ~~of~~ the inflow function i(t) by means of values determined from said pulsatile component of said single input signal.

4. The device according to claim 1, wherein each iteration step in iteratively determining ~~the iterative determination of~~ the inflow function i(t) comprises a step-by-step calculation by approximation of the inflow function i(t) according to the equation

$$i(t) = d/dt\ (C_{tissue}(t)) + o(t-t_k)$$

and an outflow function o(t) by means of a convolution integral

$$o(t)=i(t)*g(t)$$

wherein $d/dt\ (C_{tissue}(t))$ is a term that describes a change in the injected indicator concentration with reference to the organ tissue, a value of the outflow function o(t) at a time $t-t_k$ is to be inserted for $o(t-t_k)$, and g(t) is a characteristic transport function in which the mean transit time mtt is included.

5. The device according to claim 1, wherein the stop criterion for iteratively determining ~~the iterative determination of~~ the inflow function i(t) includes that a minimum of the inflow function i(t), determined by means of iteration, is greater than a threshold value.

7. The device according to claim 4, wherein the stop criterion for iteratively determining ~~the iterative determination of~~ the inflow function i(t) includes that the inflow function i(t) can be represented as a sum of a finite number of functions that are similar in form to the transport function g(t).

8. (Cancelled)

9. The device according to claim 1, further comprising a non-invasive measurer of blood flow in the organ including means for radiating near infrared radiation in through ~~the~~ a patient's skin at the first location and means for capturing the exiting proportion of the emitted near infrared radiation through the patient's skin at the second location.

12. (Cancelled)

13. A method for measuring blood flow in an organ of a patient ~~using an injected indicator~~ comprising the steps of:

injecting the patient with an indicator;

emitting near infrared radiation into tissue of the organ at a first location;

detecting a proportion of the emitted near infrared radiation that exits from the organ at a second location as a single input signal;

dividing up said single input signal into a pulsatile component and a non-pulsatile component;

determining an ~~determination of~~ injected indicator concentration with reference to the organ tissue from said non-pulsatile component of said single input signal;

iteratively determining ~~iterative determination~~, from said non-pulsatile component, ~~of~~ an inflow function i(t) that characterizes blood flow through the organ by incrementally varying a mean transit time mtt until a stop criterion is reached;

determining an ~~determination of~~ injected indicator concentration with reference to blood volume in the organ from said pulsatile component of said single input signal and the iteratively determined inflow function i(t);

calculating a ~~calculation of~~ blood volume in the organ as a quotient of the blood volume in the organ and the mean transit time mtt when the stop criterion has been reached.

calculating a ~~calculation of the~~ blood flow in the organ as a quotient of the blood volume in the organ and the mean transit time mtt when the stop criterion has been reached.

14. A method for measuring blood flow in an organ ~~using an injected indicator~~ comprising the steps of:

injecting an indicator;

emitting near infrared radiation, into tissue of the organ at a first location;

detecting a proportion of the emitted near infrared radiation that exits from the organ at a second location as a single input signal;

dividing up said single input signal into a pulsatile component and a non-pulsatile component;

determining an ~~determination of~~ injected indicator concentration with reference to the organ tissue from said non-pulsatile component of said single input signal;

iteratively determining ~~iterative determination~~, from said non-pulsatile component, ~~of~~ an inflow function i(t) that characterizes blood flow through the organ by incrementally varying a mean transit time mtt until a stop criterion is reached;

determining an ~~determination of~~ injected indicator concentration with reference to blood volume in the organ from said pulsatile component of said single input signal and the iteratively determined inflow function i(t);

calculating a ~~calculation of~~ blood volume in the organ as a quotient of the injected indicator concentration with reference to the organ tissue and the injected indicator concentration with reference to the blood volume in the organ;

calculating a ~~calculation of the~~ blood flow in the organ as a quotient of the blood volume in the organ and the mean transit time mtt when the stop criterion has been reached; and

scaling the inflow function i(t) by means of values determined from said pulsatile component of said single input signal.

15. The method according to claim 14, wherein the step of determining ~~the determination of~~ the concentration of injected indicator with reference to the blood volume in the organ comprises back-extrapolating ~~back extrapolation of~~ the scaled inflow function i(t) to a time of injection of the indicator.

16. The method according to claim 13, wherein each iteration step in iteratively determining ~~the iterative determination of~~ the inflow function i(t) comprises a step-by-step calculation by approximation of the inflow function i(t) according to the equation

$$i(t) = d/dt\ (C_{tissue}(t)) + o(t - t_k)$$

and of an outflow function o(t) by means of a convolution integral

$$o(t) = i(t) * g(t)$$

wherein $d/dt\ (C_{tissue}(t))$ is a term that describes a change in the injected indicator concentration with reference to the organ tissue, a value of the outflow function o(t) at a time $t - t_k$ is to be inserted for $o(t-t_k)$, and g(t) is a characteristic transport function in which the mean transit time mtt is included.

17. The method according to claim 13, wherein the stop criterion for iteratively determining ~~the iterative determination of~~ the inflow function i(t) includes that a minimum of the inflow function i(t) determined by means of iteration is greater than a threshold value.

19. The method according to claim 16, wherein the stop criterion for iteratively determining ~~the iterative determination of~~ the inflow function i(t) includes that the inflow function i(t) can be represented as a sum of a finite number of functions that are similar in form to the transport function g(t).

20. The method according to claim 13, wherein the indicator has an absorption coefficient ~~of the indicator~~ that decreases with an increasing indicator concentration and the absorption coefficient is used ~~is stated~~ for determining ~~the determination of~~ the injected indicator concentration with reference to the blood volume in the organ.

21. The method according to claim 13, wherein a skin perfusion is reduced at the first location and the second location by means of applying a locally increased contact pressure.

22. The method according to claim 13, wherein the organ is ~~a patient's~~ the brain, the blood flow is cerebral blood flow CBF, and the blood volume is cerebral blood volume CBV.

24. A device for measuring blood flow in an organ using an injected indicator comprising:

a radiation source for emitting near infrared radiation into tissue of the organ at a first location;

a sensor for detecting a proportion of the emitted near infrared radiation that exits from the organ at a second location; and

an evaluation unit that detects the proportion of the emitted near infrared radiation that exits from tissue of the organ as a single input signal, said evaluation unit being programmed to perform the following evaluation steps:

(a) dividing up said single input signal into a pulsatile and a non-pulsatile component;

(b) determining an ~~determination of~~ injected indicator concentration with reference to the organ tissue from said non-pulsatile component of said single input signal;

(c) iteratively determining ~~iterative determination~~, from said non-pulsatile component, ~~of~~ an inflow function i(t) that characterizes blood flow through the organ by incrementally varying a mean transit time mtt until a stop criterion is reached;

(d) determining an ~~determination of~~ injected indicator concentration with reference to blood volume in the organ from said pulsatile component of said single input signal and the iteratively determined inflow function i(t);

(e) scaling ~~of~~ the inflow function i(t) by means of values determined from said pulsatile component of said single input signal;

(f) back-extrapolating ~~back extrapolation of~~ the scaled inflow function i(t) to a time of injection of the indicator;

(g) calculating a ~~calculation of~~ blood volume in the organ as a quotient of the injected indicator concentration with reference to the organ tissue and the injected indicator concentration with reference to the blood volume in the organ; and

(h) calculating a ~~calculation of the~~ blood flow in the organ as a quotient of the blood volume in the organ and the mean transit time mtt when the stop criterion has been reached.

25. (new) A method according to claim 14, wherein the indicator is indocyaningreen.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amanda L. Lauritzen whose telephone number is (571)272-4303. The examiner can normally be reached on Monday - Friday, 8:30am - 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brian L. Casler can be reached on (571) 272-4956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Amanda L. Lauritzen/
Examiner, Art Unit 3737

/Ruth S. Smith/
Primary Examiner, Art Unit 3737